Attorney Docket No.: 10022.204-US **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Jørgensen et al.

Serial No.: To be assigned

Confirmation No: To be assigned

Group Art Unit: To be assigned

Filed: August 13, 2001

Examiner: To be assigned

For: Method For Stable Chromosomal Multi-Copy Integration Of Genes

PRELIMINARY AMENDMENT

Commissioner for Patents Washington, DC 20231

Sir:

Before the above-captioned application is taken up for examination, entry of the following amendment is respectfully requested:

IN THE CLAIMS:

Please cancel claims 6-29, 45-62 and 64-65 without prejudice or disclaimer.

Please substitute the following amended claims for the pending claims having the same claim numbers:

- 3. The method of claim 1, wherein subsequent to the step of introducing the DNA construct and cultivating the cell under selective conditions, or subsequent to the step of selecting a host cell, a second recombination takes place between the DNA fragment and the homologous host cell DNA sequence.
- 44. A host cell comprising at least two copies of a gene of interest stably integrated into the chromosome, where at least one copy is integrated adjacent to a conditionally essential locus and wherein the cell is obtainable by the method of claim 1.
- 66. A process for producing an enzyme of interest, comprising cultivating a cell of claim 44 under conditions appropriate for producing the enzyme, and optionally purifying the enzyme.

REMARKS

This amendment is submitted to cancel claims in order to reduce the filing fee. Claims 3, 44 and 66 have been amended to remove multiple dependencies. There is no new matter added, and entry of the amendment is respectfully requested.

This application contains a Sequence Listing. Applicants enclose a 3.5" floppy disk containing the Sequence Listing. The content of the attached paper entitled "SEQUENCE LISTING" and of the accompanying identically labelled diskette is the same.

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: August 13, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Sir:

Below is a marked-up version of the amendments made in the accompanying amendment.

IN THE CLAIMS:

Claims 3, 44 and 66 have been amended as follows:

- 3. The method of claim 1—er—2, wherein subsequent to the step of introducing the DNA construct and cultivating the cell under selective conditions, or subsequent to the step of selecting a host cell, a second recombination takes place between the DNA fragment and the homologous host cell DNA sequence.
- 44. A host cell comprising at least two copies of a gene of interest stably integrated into the chromosome, where at least one copy is integrated adjacent to a conditionally essential *locus* and wherein the cell is obtainable by any of the methods defined in of claims 1—29.
- 66. A process for producing an enzyme of interest, comprising cultivating a cell as defined in any of claims 44 62 under conditions appropriate for producing the enzyme, and optionally purifying the enzyme.